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Comparative Analysis of Dose Variations in Tumor Volumes and Organs at Risk in IMRT Plans for Head-And – Neck, Pelvis and Brain Cancers with Varying Dose Calculation Grid Sizes

Pathak P[1]*, Guha S[2], Vitwekar Vidya[3], Majumder Sourav[4] and Soni Ashok[5]

[1]*Chief medical Physicist, BIMR Hospitals, Gwalior, India*
[2]*Radiation Oncologist, Tata Medical Center, Kolkata, India*
[3]*Radiotherapy Technologist, Rajiv Gandhi University of Health Sciences, India*
[4]*Diploma in Radiotherapy Technology, Radiotherapy Technologist, India*
[5]*Service Engineer, BIMR Hospitals, Gwalior, India*

Abstract

Purpose: The aim of this study was to compare the plan results that were obtained by using different calculation grid sizes ranging from 3 mm to 10 mm, and the same dose calculation algorithm Pencil Beam (PB), in Intensity Modulated Radiotherapy (IMRT) for different treatment sites Head-And –Neck, Pelvis (Carcinoma Cervix) And Brain Cancers.

Introduction: Ever since the advent and development of treatment planning systems, the uncertainty associated with calculation grid size has been an issue. Even to this day, with highly sophisticated 3D conformal and intensity-modulated radiation therapy (IMRT) treatment planning systems (TPS), dose uncertainty due to grid size is still a concern.

Materials and methods: Twelve patients in which four patients of Head-And –Neck, Pelvis And Brain tumors respectively were considered for the study. IMRT Plans were generated for a 6,600cGy, 5,000cGy & 5,400cGy prescribed doses for Head-And –Neck, Pelvis and Brain tumors respectively using Oncentra v 4.3 TPS. For each patient, dose calculation with Pencil Beam (PB) algorithms using dose grid sizes of 3.0 mm, 5.0 mm, and 10.0 mm were performed.

Results: The plans were evaluated as per the ICRU guidelines and dose constraints were maintained as per the Quantec guidelines. The dose differences for the varying grid sizes in Tumor Volumes and Organs at Risk were analyzed and tabulated.

Conclusion: Overall, the effect of varying grid size on dose variation appears to be insignificant. However, 3 mm is recommended to ensure acceptable dose calculations, especially in high gradient regions.

Keywords: Dose grid; 2D Array; Organs at risk; Intensity-modulated radiotherapy; Dose-volume changes; Head-and-neck cancers

Introduction

The benefit of intensity-modulated radiation therapy (IMRT) in the treatment of head-and-neck cancer (HNC) has been demonstrated in numerous studies [1-3]. Highly conformal radiation allows for a high dose to high-risk areas, whilst sparing adjacent organs at risk (OAR) such as the parotid glands. Clinical studies have shown that IMRT reduces grade-3 xerostomia comparison to three-dimensional conformal radiotherapy (3D CRT) [4,5], for that reason IMRT has become the standard treatment in many centers. IMRT dose distributions, with steep dose gradients, are very sensitive to geometrical uncertainties, and hence, deviations between planned and delivered dose distributions have to be minimized. One way of improving the treatment accuracy is to reduce geometrical errors. Rigid errors, such as setup, have been extensively studied. Mechalakos et al. [6]. for instance evaluated the interfraction and interfraction errors in treatments of HNC and compared their results with previous studies from others authors. Margins are added to clinical volumes in order to take into account geometrical uncertainties. These planning margins are commonly calculated from measured systematic and random geometrical errors [7].

However, it is well known that many HNC patients treated with radiotherapy (RT) suffer significant anatomical changes due to tumor shrinkage or weight loss. Several scheduled rescanning studies have evaluated these volumetric changes in both target volumes and normal tissues [8-11], mostly on the parotid glands and their consequent effects on dose distribution [12-15].

The purpose of the present study was to analyze the variation on the dose distribution in Planning target volumes (PTVs) and organs at risk (OAR). The use of IMRT implies the irradiation of more OARs than conventional 3D CRT. Therefore, beside typical susceptible organs such as the eyes, optic nerves, optic chiasm, spinal cord, parotid glands, bladder, rectum and bowel we have also included additional OARs such as the brainstem, and femur head.

The IMRT technique has the potential benefit over conventional

***Corresponding author:** Pathak P, Chief medical Physicist, BIMR Hospitals, Radiation Oncology, Surya mandir road Gwalior, Madhya Pradesh 474004, India, Tel: 07512405715; E-mail: pankaj2002@hotmail.com

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whole-pelvis irradiation of improving target dose coverage, reducing the volume of the organs at risk (OARs) that receive irradiation, and reducing the toxicity to normal tissue [16-19]. Despite the significant benefits of IMRT, there are some disadvantages. The technique usually requires multiple fixed-angle radiation beams, which can increase treatment delivery time. This has an impact on patient comfort, reproducibility of the treatment position, and intra-fraction motion. Moreover, IMRT uses a larger number of monitor units (MUs) compared with conventional conformal radiotherapy (CRT), leading to an increase in the amount of low-dose radiation received by the rest of the body. This raises the concern of secondary radiation-induced malignancy, which is of particular relevance to young patients or those with long future life expectancies [20-23].

In the past, whole-brain radiotherapy (WBRT) planning was simple. Today, new clinical and dosimetric considerations are taken into consideration when approaching such planning. It has been found that as many as 11% of patients who were treated by WBRT and survived more than 12 months developed dementia, especially with the use of a larger dose-per-fraction regimen [24]. However, regression of the lesions after WBRT was found to correlate with survival and improved neurocognitive function. Therefore, achievement of macroscopic lesion control is the mainstay of treatment. Thus, treatment-dose compromise is unjust for preserving these neurocognitive functions. Furthermore, memory functions were found to be most susceptible to early decline, even in patients with nonprogressing brain metastases [25]. These concerns became more significant as WBRT was instituted for prophylactic brain irradiation (PCI) for various neoplasms to decrease intracranial failure in patients with potential long-term survival [26].

In the case of IMRT, this is accomplished by using complex computer models to calculate the dose to a given volume. These volumes and their resolution of defined by the calculation grid, which defines the space where the dose calculation models are applied and the resolution of that space. However, the calculation grid has been generally left at a default value to minimize the amount of time that the treatment planning system needs to perform the dose calculations. The intent of the project is, therefore, to test the effect of very fine calculation grid resolutions on the accuracy of IMRT plans.

The intent of the study is, therefore, to test the effect of calculation grid sizes on the accuracy of IMRT plans.

Materials and Methods

C T acquisition and contouring

CT scans were acquired using a Somatom Power Spirit CT Simulator (Siemens) with 3–5 mm slice spacing. Patients were in the supine position and immobilized with a thermoplastic head–shoulder mask. A planning CT scan (CT) was acquired one week before RT treatment. The Oncentra version 4.3 (Nucletron) treatment planning system was used for delineation and dose distribution calculations. Target volumes and normal tissues were manually contoured by a physician on each axial slice of the CT using MRI or contrast-enhanced CT. The definition of volumes was in accordance with ICRU Reports 50-62, but dose-volume parameters were reported according to the new ICRU Report 83 IMRT recommendations. Gross tumor volume (GTV) included the primary tumor and affected lymph nodes. The GTV was expanded to include the high-risk regions (CTV).

To compensate for geometrical uncertainties such as setup and organ motion, a 5 mm margin was automatically added to CTVs to obtain the planning target volume (PTV). In order to avoid dose compensation in the build-up region, in cases with no skin infiltration, the PTVs were manually modified excluding areas where the distance to the skin was less than 3 mm. Although these modified PTVs were used during optimization process, the absorbed dose was reported over the whole PTV. Prescribed doses were 6,600cGy, 5,000cGy & 5,400cGy for HEAD-AND –NECK, PELVIS (Carcinoma Cervix), & BRAIN respectively.

The critical structures contoured were: the parotid glands, spinal cord, mandible, eyes, oral cavity, brainstem, brain, optic nerves, optic chiasm, bladder, rectum, bowel & femur heads.

Treatment planning

IMRT treatment plans were generated on the CT with nine 6 MV

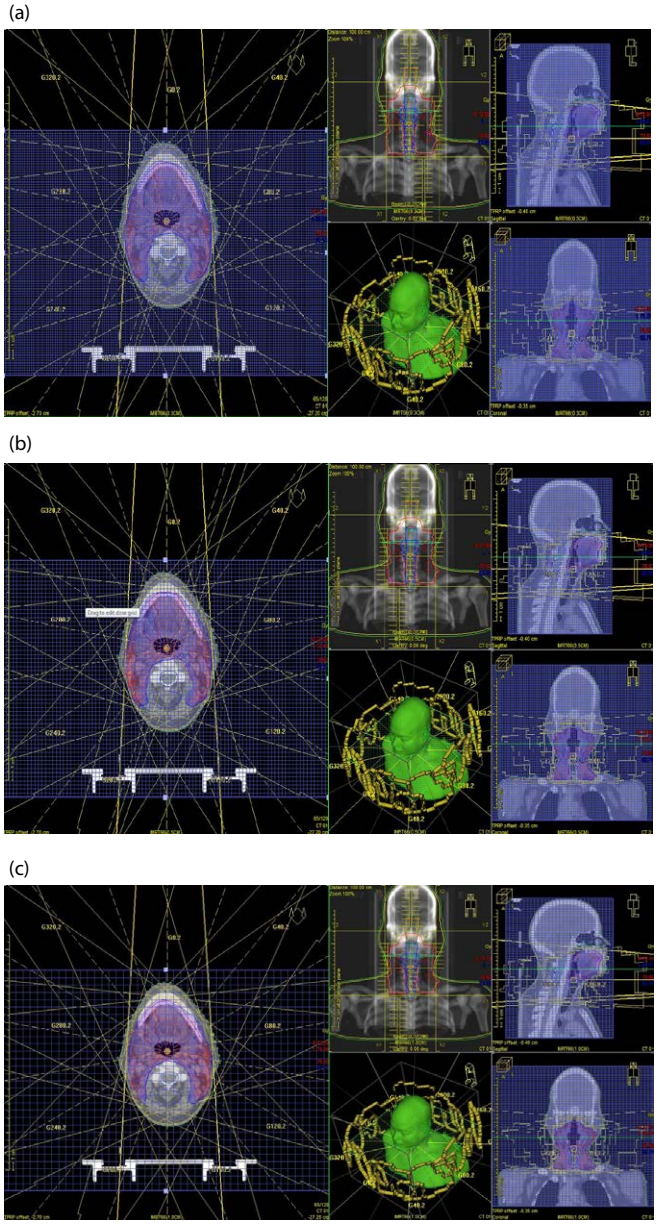

Figure 1: Showing 95% Isodose distribution In Head & Neck Cancer. (a) With 3mm Dose Calculation Grid Size (b) With 5mm Dose Calculation Grid Size (c) With 10mm Dose Calculation Grid Size.

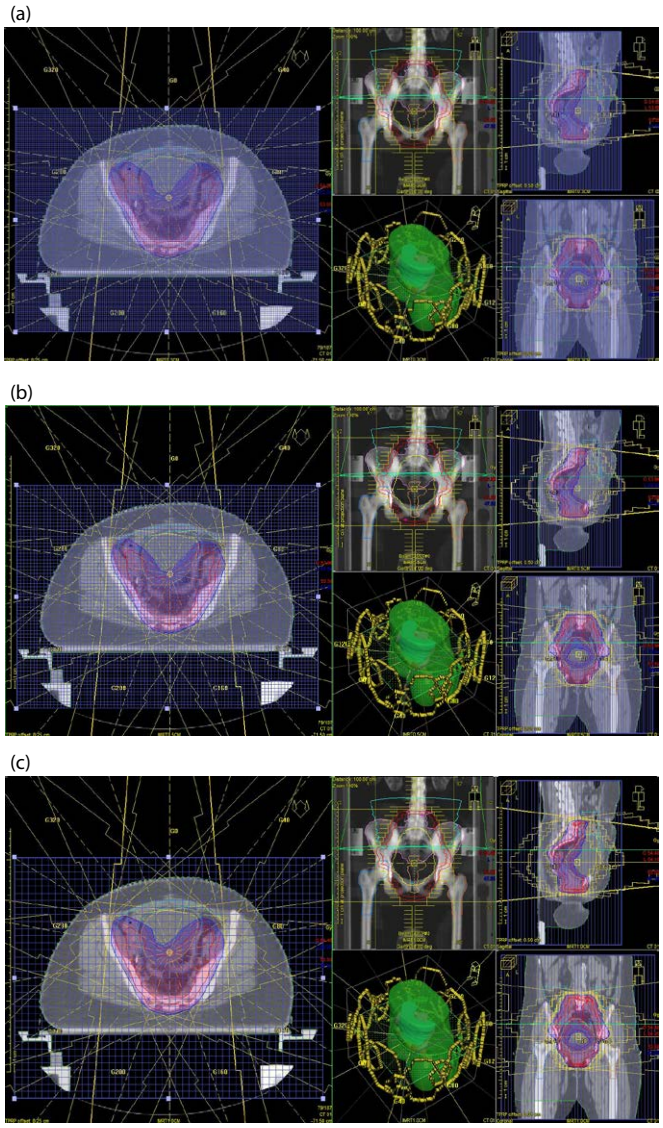

Figure 2: Showing 95% Isodose distribution In Pelvis (Carcinoma Cervix) Cancer. (a) With 3mm Dose Calculation Grid Size (b) With 5 mm Dose Calculation Grid Size (c) With 10 mm Dose Calculation Grid Size.

fields on the Oncentra treatment planning system. For each of the calculation grid sizes, three different sites; namely, Head -And- Neck, Cervix, and Brain were analyzed as shown in Figures 1(a) (b) (c), 2(a) (b) (c) and 3(a) (b) (c). The IMRT plans were optimized using an inverse planning algorithm. The final dose distribution was calculated using the Pencil Beam (PB) with heterogeneity correction and 3-10 mm grid resolution. Dose volume histograms were generated for each of the cases and statistical analysis performed included mean relative difference and Homogeneity Index for target structures. Comparison was done first by using 3mm calculation grid as a golden standard and keeping the same number of monitor units (MUs) per beam for each grid size, then the second part involved renormalizing plans to have the same target coverage (95% of the prescription dose covering at least 95% of the target volume) for each grid size used shown in Table 1 (a), (b) and (c).

Future study plans include their verification with the PTW 2D Array.

Optimization goals were as follows: 1) prescription doses (Dpres) must encompass at least 95% of target volumes; 2) near-minimum absorbed doses (D98%) of PTVs should be higher than 92% of Dpres; 3) the near-maximum absorbed dose (D2%) of the PTVs should be less than 110% of Dpres.

High priority constraints to normal critical structures were: no more than 1.0 cm^3 of spinal cord could receive more than 46 Gy ; 2) no more than 1% of brainstem could receive more 54Gy; 3) the parotid gland volume receiving 26Gy should be less than 50% in at least one gland; 4) optic nerves Dmax should be less than 56Gy 5)optic chiasm Dmax should be less than 54Gy 6) Bowel 195cc should be less than 45Gy; 7) bladder Dmax should be less than 45Gy; 8) Rectum Dmax should be less than 50Gy; 9) D2% of normal tissue should be less than Dpres.

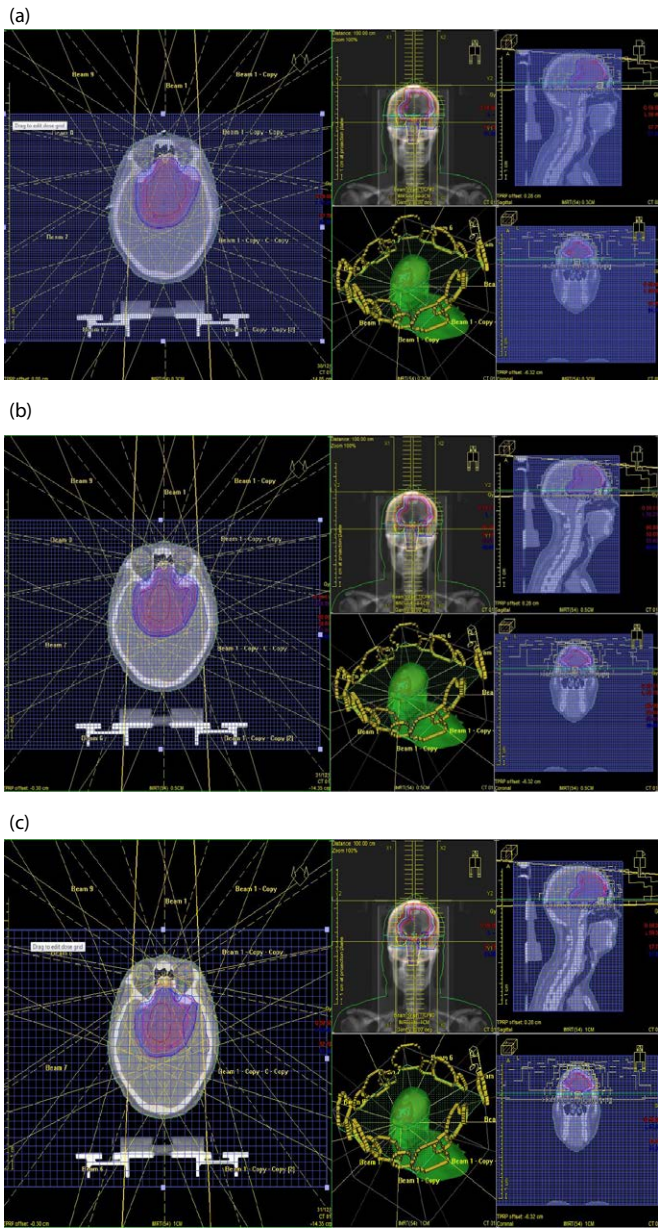

Figure 3: Showing 95% Isodose distribution In Brain Cancer. (a) With 3mm Dose Calculation Grid Size (b) With 5 mm Dose Calculation Grid Size (c) With 10 mm Dose Calculation Grid Size.

Head-And-Neck(66Gy/33#)									
Grid Sizes(mm)									
Cases	3.0			5.0			10.0		
	V95%	V107%	V110%	V95%	V107%	V110%	V95%	V107%	V110%
Case1	96.18%	1.39%	0.13%	96.03%	1.85%	0.25%	95.01%	1.78	0.09%
Case2	95.55%	0.11%	0.00%	95.45%	0.96%	0.03%	95.22%	0.15%	0.00%
Case3	95.07%	1.23%	0.06%	95.72%	3.24%	0.66%	95.40%	2.75%	0.00%
Case4	95.56%	0.30%	0.00%	95.05%	1.85%	0.39%	95.22%	0.59%	0.00%
Avg.	95.59%	0.76%	0.05%	95.56%	1.98%	0.33%	95.21%	1.32%	0.02%
Std.Dev	0.2470	0.5690	0.6180	0.4030	0.9410	0.2630	0.1590	0.118	0.420

(a)

Pelvis(Carcinoma Cervix)[50Gy/25#]									
Grid Sizes(mm)									
Cases	3.0			5.0			10.0		
	V95%	V107%	V110%	V95%	V107%	V110%	V95%	V107%	V110%
Case1	97.79%	0.31%	0.00%	97.75%	0.38%	0.00%	96.86%	0.17%	0.00%
Case2	96.07%	0.27%	0.00%	96.09%	0.17%	0.00%	96.13%	0.99%	0.00%
Case3	95.58%	0.84%	0.00%	95.59%	0.23%	0.00%	95.49%	1.00%	0.00%
Case4	96.02%	0.20%	0.01%	95.26%	0.08%	0.00%	95.14%	0.65%	0.30%
Avg.	96.37%	0.41%	0.00%	96.17%	0.22%	0.00%	95.91%	0.70%	0.08%
Std.Dev	0.9751	0.2924	0.0050	1.1056	0.1260	0.0000	0.7572	0.3905	0.15

(b)

Brain(54Gy/27#)									
Grid Sizes(mm)									
Cases	3.0			5.0			10.0		
	V95%	V107%	V110%	V95%	V107%	V110%	V95%	V107%	V110%
Case1	98.33%	0.00%	**0.00%**	98.56%	0.27%	**0.00%**	96.16%	0.95%	**0.15%**
Case2	96.80%	1.13%	**0.00%**	96.08%	1.39%	**0.00%**	95.02%	3.25%	**0.37%**
Case3	95.41%	1.42%	**0.00%**	95.30%	3.22%	**0.02%**	95.31%	2.55%	**0.00%**
Case4	95.15%	2.34%	**0.20%**	95.17%	2.97%	**0.25%**	95.44%	2.19%	**0.16%**
Avg.	96.42%	1.22%	0.05%	96.28%	1.96%	0.07%	95.48%	2.24%	0.17%
Std.Dev	1.4634	0.9645	0.0946	1.5738	1.3890	0.1220	0.4845	0.8340	0.152

(c)

Table 1: (a), (b) and (c) shows target volume averaged dose parameters at CT with varying grid sizes for different sites viz. Head & Neck, Pelvis & Brain. Values are presented as a percentage of Dpres of PTV.

Low priority constraints that should not compromise target coverage were: 1) eyes Dmax should be less than 50 Gy.

Results

The maximum percentage of variation recorded between calculation grid sizes used was in the case of the Head and Neck treatments. For the Cervix and Brain cases there was little variation in the results based on the calculation grid size chosen. However head and neck cases with nodal involvement showed significant variation in the dosimetric results based on the grid size chosen as shown in Table 2 (a), (b) and (c). Overall results vary from case to case and also depend on the plan complexity. For larger treatment areas calculating with the grid size smaller than 3mm may be impossible as time needed for calculation rises exponentially with the field size involved. In gamma function tests, all grid sizes met the criteria of acceptability. (i.e., 95% of the region resulted in gamma index less or equal to 1 with a 3% dose difference and a 3 mm Distance to target agreement (DTA) criteria) except for deep target and 5 mm and 10 mm grid sizes where 95% of the region resulted in gamma index less or equal to 1 with a 5% dose difference and a 5 mm DTA criteria. It was observed that larger grid spacing produces higher dose gradient.

There are enduring uncertainties regarding the optimal dose grid resolution for use with pelvic intensity-modulated radiotherapy (IMRT) plans in which the adjacent organs at risk are slender and transect the field edge

Table 1 (a), (b) and (c) shows target volume averaged dose parameters at CT with varying grid sizes for different sites viz. Head & Neck, Pelvis & Brain. Values are presented as a percentage of Dpres of PTV.

Conclusions

IMRT places a higher requirement on dose grid resolution than conventional radiation therapy. While 3 mm-5 mm grid was assumed adequate for conformal treatment planning, smaller dose grid is required at least in the areas of high dose. In the cases where steep dose gradients exist smaller grid size should be used while calculating and evaluating treatment plans, as the choice of the calculation grid size may in certain cases even influence clinical results. The statistical analysis showed that there were no significant differences in conformity & homogeneity except in some cases of 10 mm grid size IMRT plan as shown in Table 3 (a), (b) and (c). The CI for all the sites were 0.95 which shows that even if the grid sizes are chosen from 3 mm-10 mm the plans are conformal enough to be accepted for delivery ,but it requires little optimization for 5mm-10 mm . The average HI for Head & Neck, Pelvis & Brain are 0.135,0.1175,0.13 for 3 mm , 0.1475,0.12,0.14 for 5 mm & 0.165,0.1325,0.157 for 10 mm which shows that the plans are

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Head-And-Neck(66Gy/33#)									
Grid Sizes(mm)									
Organs At Risk	3.0			5.0			10.0		
	D1cc (Gy)	Dmax (Gy)	Mean Dose (Gy)	D1cc (Gy)	Dmax (Gy)	Mean Dose (Gy)	D1cc (Gy)	Dmax (Gy)	Mean Dose (Gy)
Spinal Cord									
Case1	40.18	43.50			43.24		44.93	42.16	
Case2	44.26	46.84			45.59		46.18	46.45	
Case3	40.72	43.19			44.87		45.11	45.11	
Case4	43.19	46.05			42.54		44.89	41.56	
Spinal cord PRV									
Case1	47.59	49.72			48.84		49.42	47.01	
Case2	48.22	50.89			47.01		48.48	46.53	
Case3	48.14	49.69			48.97		51.81	47.33	
Case4	48.42	51.72			49.98		48.76	47.50	
Brain Stem									
Case1	40.40	47.07		39.60	44.00		44.77	46.91	
Case2	32.83	38.32		32.90	36.78		33.06	35.02	
Case3	51.66	53.95		52.77	54.86		53.44	54.76	
Case4	45.31	49.68		45.38	50.42		49.50	49.88	
Brain Stem PRV									
Case1	47.42	56.24			52.40		49.86	53.84	
Case2	36.40	40.53			40.16		36.57	36.48	
Case3	55.65	59.58			59.87		56.35	57.10	
Case4	55.15	55.15			56.21		59.26	59.26	
Parotid									
Case1			35.42			34.49			31.97
Case2			35.42			34.50			32.50
Case3			33.40			34.50			35.00
Case4			34.50			38.83			40.00

(a)

Pelvis(Carcinoma Cervix)[50Gy/25#]									
Grid Sizes(mm)									
Organs At Risk	3.0			5.0			10.0		
	D1cc (Gy)	Dmax (Gy)	Mean Dose (Gy)	D1cc (Gy)	Dmax (Gy)	Mean Dose (Gy)	D1cc (Gy)	Dmax (Gy)	Mean Dose (Gy)
Bladder									
Case1	50.94	51.29		51.70	52.02		52.04	52.04	
Case2	50.50	51.00		50.57	50.94		51.58	51.56	
Case3	51.82	52.09		51.18	51.71		52.84	52.94	
Case4	49.85	50.25		50.51	50.83		50.64	50.68	
Rectum									
Case1	52.14	52.63		52.71	53.10		52.75	53.05	
Case2	50.15	50.99		50.79	51.62		50.88	50.92	
Case3	52.38	52.62		51.40	51.90		52.78	52.68	
Case4	50.98	51.54		51.35	51.67		51.48	51.59	
Rt.FH									
Case1		44.53			44.64			45.13	
Case2		50.55			50.86			50.12	
Case3		50.82			49.21			47.08	
Case4		46.96			46.01			41.5	
Lt.FH									
Case1		44.59			44.56			45.70	
Case2		51.15			50.75			53.62	
Case3		51.60			50.64			51.18	
Case4		48.01			45.26			43.56	
Bowel	D195cc (Gy)	Dmax (Gy)	Mean Dose (Gy)	D195cc(Gy)	Dmax (Gy)	Mean Dose (Gy)	D195cc(Gy)	Dmax (Gy)	Mean Dose (Gy)
Case1	41.62	53.47		41.93	52.74		41.73	51.73	
Case2	39.77	53.65		39.30	53.56		39.62	53.62	
Case3	45.29	53.48		45.04	52.49		46.17	53.41	
Case4	42.47	53.37		42.34	53.85		42.99	52.19	

(b)

Brain(54Gy/27#)									
Grid Size (mm)									
Organs at Risk	3			5			10		
	D1cc (Gy)	Dmax (GY)	Mean Dose(GY)	D1cc (Gy)	Dmax (GY)	Mean Dose(GY)	D1cc (Gy)	Dmax (GY)	Mean Dose (GY)
optic chiasm									
Case1	20.11	29.32		21.13	26.98		21.57	28.36	
Case2	53.0	53.82		51.39	55.21		51.39	53.69	
Case3	51.21	55.23		51.39	55.21		51.48	55.33	

Case4	35.66	49.65		35.74	46.96		35.07	46.96	
Optic chiasm PRV									
Case1	26.62	35.16		27.03	34.37		26.97	30.11	
Case2	53.69	55.64		55.61	57.68		53.69	57.18	
Case3	55.25	56.57		55.66	56.34		55.39	55.78	
Case4	47.36	53.10		46.97	51.87		47.88	47.50	
BRAIN STEM									
CASE1	52.17	53.36		53.28	54.76		53.23	54.75	
CASE2	52.78	59.10		54.23	55.88		55.81	56.95	
CASE3	35.75	37.28		36.02	37.23		16.77	37.04	
CASE4	54.00	54.68		53.59	53.98		54.69	55.19	
BRAIN STEMPRV									
CASE1	53.92	55.35		54.82	55.93		53.75	55.75	
CASE2	54.61	55.90		55.35	55.96		56.63	58.45	
CASE3	50.16	52.15		50.63	51.62		50.97	51.79	
CASE4	54.12	54.77		53.77	54.21		54.92	55.19	
Rt.Eye									
Case1		6.27	4.81		7.83	5.66		6.56	5.06
Case2		31.08	14.39		28.34	14.32		14.04	26.9
Case3		40.29	22.46		38.33	21.96		34.15	22.4
Case4		22.64	7.27		22.44	7.31		19.78	7.31
Lt.Eye									
Case1		17.18	15.10		17.93	15.8		17.98	16.28
Case2		44.60	19.34		42.28	19.66		38.91	15.93
Case3		40.09	20.17		38.81	19.79		33.05	19.89
Case4		15.06	4.50		14.88	4.40		14.08	4.40

(c)

Table 2: (a), (b) & (c) summarizes dose distribution changes on OAR with varying grid sizes for different sites viz. Head and Neck, Pelvis, Brain, which showed some significant variation between planning CT.

Pelvis[Ca.cervix](50Gy/25#) Grid Sizes(mm)															
Cases	3					5					10				
	D2% (Gy)	D98% (Gy)	D50% Gy)	C.I	H.I	D2% (Gy)	D98% (Gy)	D50% (Gy)	C.I	H.I	D2% (Gy)	D98% (Gy)	D50% (Gy)	C.I	H.I
Case1	52.95	46.91	50.64	0.95	0.12	52.95	46.61	50.67	0.95	0.13	53.19	46.3	50.83	0.95	0.14
Case2	52.86	47.38	50.59	0.95	0.1	52.96	47.35	50.73	0.95	0.11	52.95	46.72	50.98	0.95	0.12
Case3	53.29	46.35	51.48	0.949	0.13	52.79	46.02	50.83	0.95	0.13	53.31	46.02	51.38	0.95	0.14
Case4	52.5	46.43	50.55	0.95	0.12	51.82	46.08	50.31	0.94	0.11	52	45.64	50.54	0.95	0.13

(a)

Head And Neck(66Gy/33#) Grid Sizes(mm)															
Cases	3					5					10				
	D2% (Gy)	D98% (Gy)	D50% (Gy)	C.I	H.I	D2% (Gy)	D98% (Gy)	D50% (Gy)	C.I	H.I	D2% (Gy)	D98% (Gy)	D50%(Gy)	C.I	H.I
Case1	70.32	60.78	67.35	0.95	0.14	70.56	60.52	67.2	0.95	0.15	70.52	59.22	67.6	0.95	0.17
Case2	69.01	60.64	65.82	0.95	0.13	69.83	61.02	65.88	0.95	0.13	69.54	59.73	66.33	0.95	0.15
Case3	70.25	60.84	66.57	0.95	0.14	71.16	60.69	67.34	0.95	0.16	70.79	58.91	67.87	0.95	0.18
Case4	69.27	61.03	65.92	0.95	0.13	70.46	60.6	66.17	0.95	0.15	69.98	59.36	67.17	0.95	0.16

(b)

Brain(54Gy/27#) Grid Sizes(mm)															
Cases	3					5					10				
	D2% (Gy)	D98% (Gy)	D50% (Gy)	C.I	H.I	D2% (Gy)	D98% (Gy)	D50% (Gy)	C.I	H.I	D2% (Gy)	D98% (Gy)	D50% (Gy)	C.I	H.I
Case1	56.4	50.02	55.18	0.95	0.11	56.28	49.8	54.66	0.95	0.12	56.96	49.64	55.38	0.95	0.13
Case2	57.52	50.15	54.68	0.95	0.13	57.61	49.72	54.25	0.95	0.14	58.13	48.78	54.4	0.95	0.17
Case3	57.61	50.17	55.4	0.95	0.13	58.07	50.18	55.33	0.95	0.14	57.93	50.02	54.54	0.95	0.14
Case4	57.91	49.69	53.67	0.95	0.15	58.13	49.65	53.79	0.95	0.16	57.87	47.57	54.7	0.95	0.19

(c)

Table 3: (a), (b) & (c) above shows statistical analysis of the IMRT plans with the Conformity Index(C.I) & Homogeneity Index(H.I) for different sites with varying grid sizes.

more homogeneous for 3 mm IMRT plans with respect to 5 & 10 mm IMRT plans .Thus 3 mm is recommended to ensure acceptable dose calculations, especially in high gradient regions.

P value and statistical significance

The two-tailed P value is less than 0.001 for target coverage.

By conventional criteria, this difference is considered to be extremely statistically significant.

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